The CTSA Program & Gene Transfer Research

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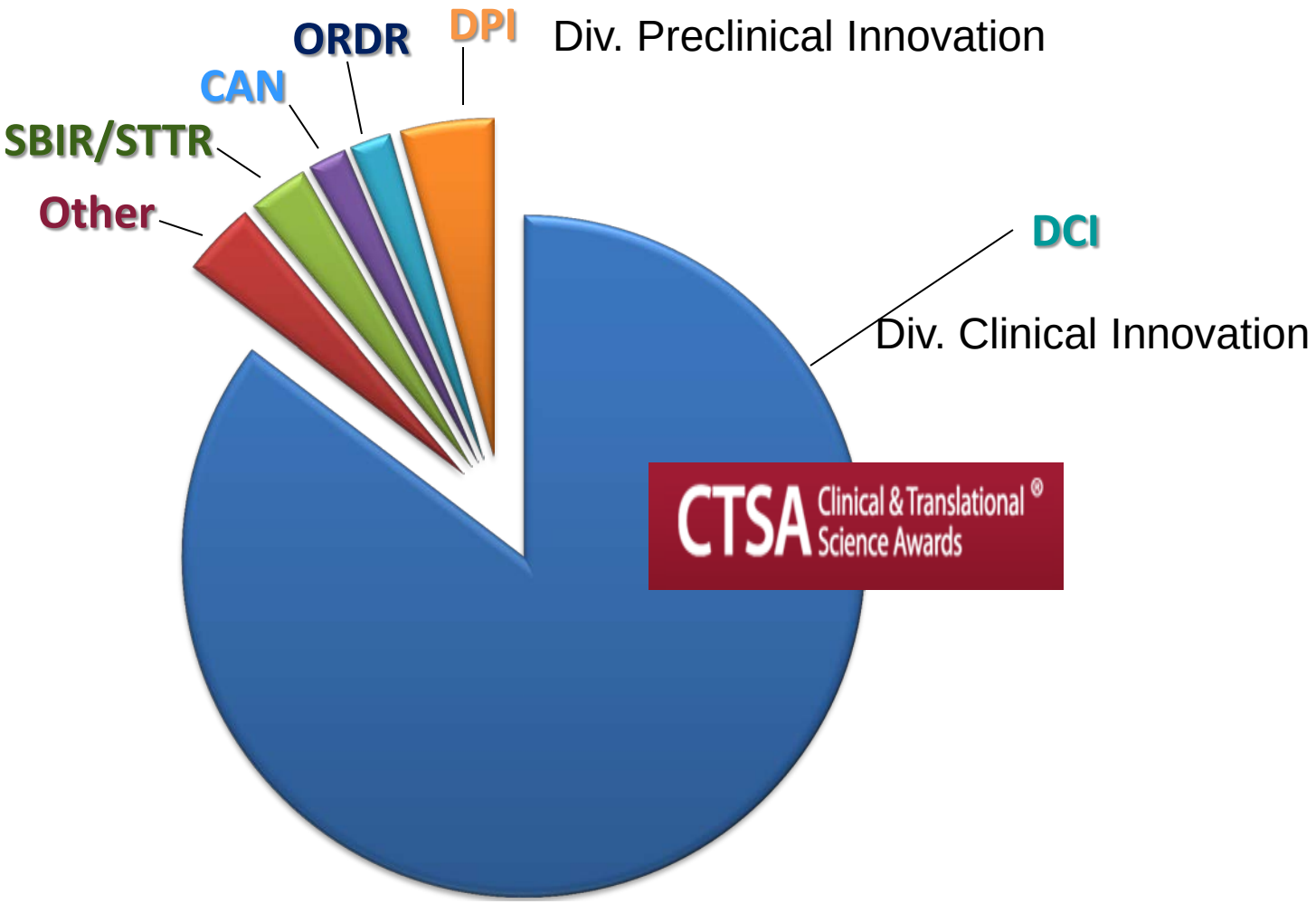
NCATS

Advancing Translational Sciences

NCATS' mission: "*... to catalyze the generation of innovative methods and technologies ... enhance the development, testing and implementation of ...diagnostics and therapeutics...*"

http://www.ncats.nih.gov/about/about.html

NCATS Research Budget – FY12 ($576M)



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- **FY 2012 budget:**
  - **NCATS Total** **$576 M**
  - **CTSA 61 sites** **$461 M**

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- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
    - **Clinical (human) need ~ potential benefit**
    - **Assay to measure effectiveness**
    - **Conception of Phase III Trial**

Advancing Translational Sciences

- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
    - **Imaging**
    - **Special technology (nano-, mass spec., novel compounds, high-end instruments)**
    - **Animal Models**
    - **Statistics, research design, epidemiology**
    - **Informatics, bio-banks, warehousing**

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- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
  - **Regulatory Requirements – development trail to license**
    - **Preclinical testing – ADME, Pharm/Tox, environment and exposure issues**
    - **Animal models**
    - **Regulatory materials, meetings, compliance, auditing**
    - **Suitable facilities, training, staff – cGMP, cGLP, cGCP**
    - **Reporting, managing, succeeding (! High failure rate)**
      - **Clinical Trials.gov Www.ClinicalTrials.gov**
      - **GemCRIS http://www.gemcris.od.nih.gov/Contents/GC_HOME.asp**

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- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
  - **Regulatory Requirements**
  - **Feasibility**
    - **Population for study – access, adequacy**
    - **Financial support**
    - **Partners (clinicians, data managers, industry) – teamwork**
    - **Environment – CRU (inpatient), Outpatient, extramural**
    - **Multisite networking – collaboration**
    - **Train of approvals (Scientific, IRB, Contracting, Budget, Nursing, Facilities)**

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- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
  - **Regulatory Requirements**
  - **Feasibility**
  - **Implementation**
    - **Protocol and informed consent document**
    - **Materials, methods, study-specific training**
    - **Study conduct, case report forms, responses to AEs and SAEs, DSMB**
    - **Enrollment, retention, study completion**

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- **How might the CTSAs support gene transfer research?**
  - **Product Concept Review**
  - **Regulatory Requirements**
  - **Feasibility**
  - **Implementation**
  - **Analysis, conclusions, publication**

Advancing Translational Sciences

- **How might the CTSAs support gene transfer research?**
- **Navigator/Manager/Concierge**
  - **Product Concept Review**
  - **Regulatory Requirements**
  - **Feasibility**
  - **Implementation**
  - **Analysis, conclusions, publication**

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- **How might the CTSAs support gene transfer research?**
- **Navigator/Manager/Concierge**
  - **Multi-disciplinary expertise – access, interest, affordability**
  - **Access to core support (materials, assays, animal handling, technology, special requirements)**
  - **Access to patient populations – electronic medical records, chronological data, engaged communities**
  - **Communication team – shaping the message, assessing effect**
  - **Consortium, collaboration, cooperation**
  - **Compliance, auditing, discipline, efficiency**
  - **Responding to challenges**

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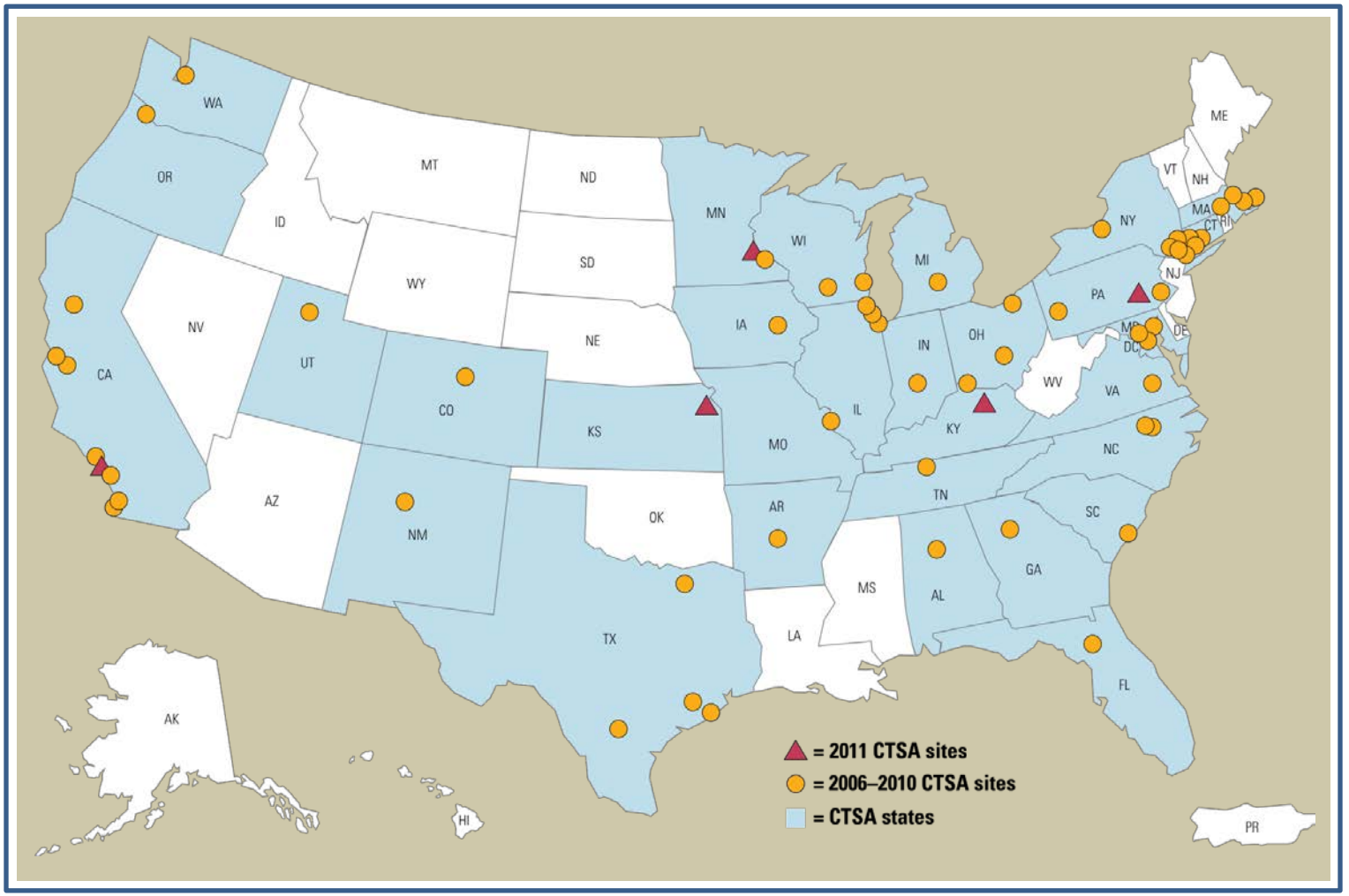
- **How might the CTSAs support gene transfer research?**
- **Navigator/Manager/Concierge**
  - **Public-private partnerships – Intellectual Property issues**
  - **Finding funds**
  - **Maintaining momentum**
- **Project Development Team**

CTSA 61 Sites: 30 States and D.C.

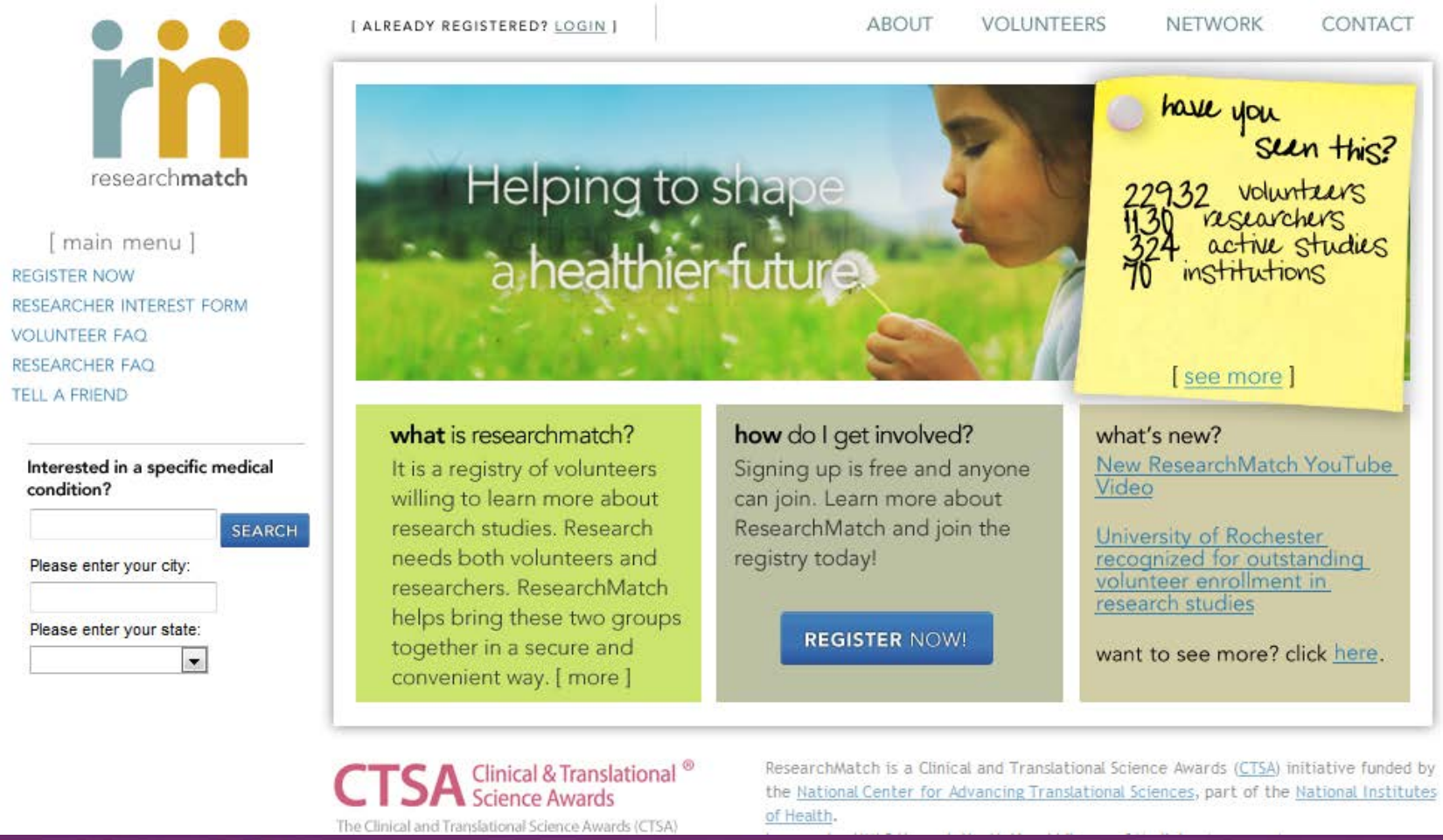


National Center for Advancing Translational Sciences

CTSA-Gene Therapy Research: Investigators at CTSA sites

- Jacobson, Hauswirth, et al. Arch Ophthalmol. *2012 Jan;130(1):9-24* Gene therapy for leber congenital amaurosis caused by RPE65 mutations: safety and efficacy in 15 children and adults followed up to 3 years. NEI U10 EY017280 & U Florida NCATS CTSI UL1 TR000064
- Flotte TR, Trapnell BC, Chulay JD et al. HUMAN GENE THERAPY 22:1239–1247 (*October 2011*) Phase 2 Clinical Trial of a Recombinant Adeno-Associated Viral Vector Expressing a1-Antitrypsin: Interim Results
- Penheiter AR, Russell SJ, Carlson SK Curr Gene Ther. *2012* Feb 1;12(1):33-47. The sodium iodide symporter (NIS) as an imaging reporter for gene, viral, and cell-based therapies

https://www.researchmatch.org/



CTSA-Gene Therapy Research: Pamela B Davis
HUMAN GENE THERAPY 23:251-253 (March 2012)

- *"An Unparalleled Engine for Discovery and Clinical Introduction: The Clinical and Translational Science Awards and Gene Therapy"*

"… [CTSA] program is intended … the main vehicle for … NIH investments in the infrastructure …for gene therapy."

- Regulatory Knowledge and support
- Participant recruitment, national and local registries, such as ResearchMatch
- Informatics
- Research Design, Biostatistics, Epidemiology, Bioethics
- Translational technologies – genomic, proteomic, metabolomic, and other biomarkers

NIH
National Center for Advancing Translational Sciences

CTSA-Gene Therapy Research:

Pamela B Davis HUMAN GENE THERAPY 23:251-253 (March 2012)

- *(continued)*
- Team develop – pre-clinical and clinical components through development, clinical testing, extension to the community
- Research navigation with special training in gene therapy, management, trained clinical investigational staff, and data coordinators
- Public Private Partnerships
- FDA requirements met: cGMP, cGLP, and cGCP facilities
- Networks for clinical trials, central data capture (REDCap), communications support, collaborative culture
- Access all CTSA websites from https://www.ctsacentral.org/

Access CTSA sites at: **https://www.ctsacentral.org/institutions**

Institutions

Currently, about 60 medical research institutions in 30 states and the District of Columbia are active members of the CTSA consortium. These institutions are working together to accelerate discoveries toward better health.

Institution Name	Year	State
Albert Einstein College of Medicine (partnering with Montefiore Medical Center) Albert Einstein-Montefiore Institute for Clinical and Translational Research	2008	NY
Boston University Boston University Clinical and Translational Science (BU-BRIDGE) Institute	2008	MA
Case Western Reserve University CTSA at Case Western University	2007	OH
Children's National Medical Center Clinical and Translational Science Institute at Children's National	2010	DC
Columbia University Irving Institute for Clinical and Translational Research	2006	NY
Duke University Duke Translational Medicine Institute	2006	NC
Emory University (partnering with Morehouse School of Medicine and Georgia Institute of Technology) Atlanta Clinical & Translational Science Institute (ACTSI)	2007	GA
Georgetown University with Howard University Georgetown-Howard Universities Center for Clinical and Translational Science	2010	DC
Harvard University Harvard Catalyst: The Harvard Clinical and Translational Science Center	2008	MA
Indiana University School of Medicine Indiana Clinical and Translational Science Institute	2008	IN

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

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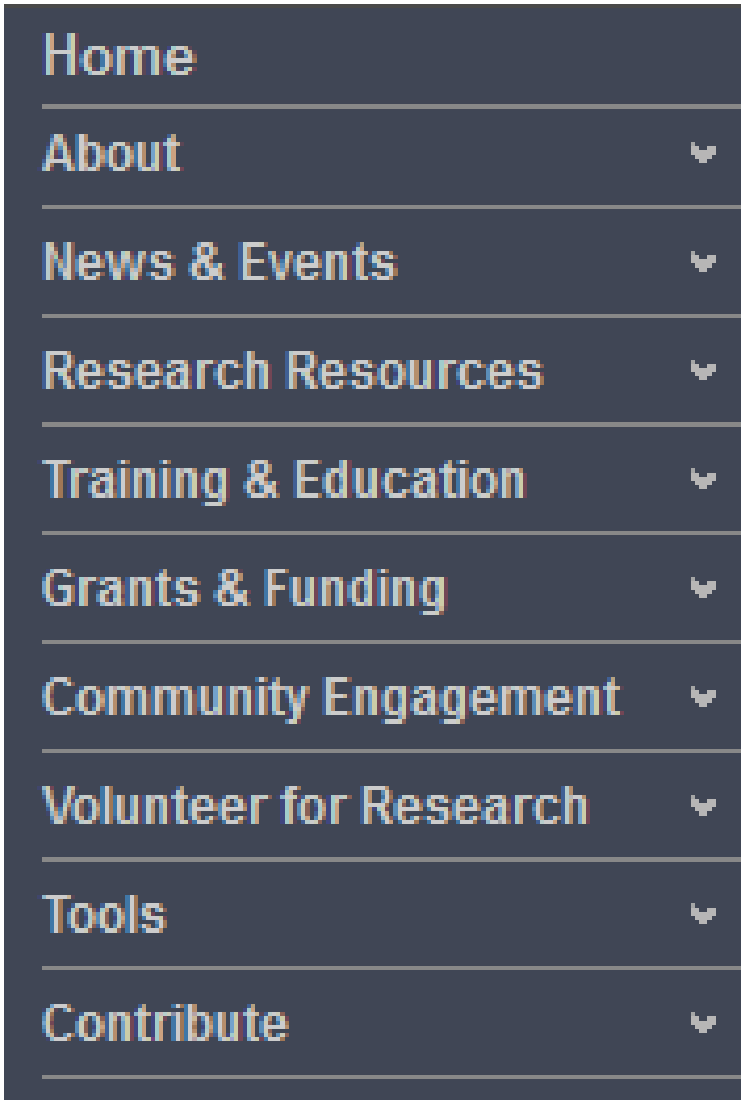
Service Menu on left side of home page on Indiana CTSA Website



Access CTSA resources at sites, example: **https://www.indianactsi.org/**

Open Drop Down → menu at Research Resources

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

- Access Technology Program (ATP) (*Indiana CTSA*)\
  - ATP Help Desk – laboratory services
  - Service cores
  - Core Pilot Grants
  - Investigational Agent Acquisition Program
  - Biobanking
  - Bioinformatics Tools

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

- Access Technology Program (ATP) (*Indiana CTSA*)\
  - ATP Help Desk – laboratory services
  - Service cores
    - Genomics
    - Proteomics
    - Informatics
    - Biostatistics
    - Research design
  - Core Pilot Grants (to help pay for core services)

- Access Technology Program (ATP) (*Indiana CTSA*)\
  - ATP Help Desk – laboratory services
  - Investigational Agent Acquisition Program
    - Assistance with regulatory submissions
    - Acquisition of
      - Pharmaceutics,
      - Nutraceuticals,
      - Placebos
    - Support for pre-clinical and clinical Pharm/Tox studies
    - Documentation
    - Compliance with FDA and other reporting requirements
    - Budgets
    - Manufacture

- Access Technology Program (ATP) (*Indiana CTSA*)\
  - ATP Help Desk – laboratory services
  - Investigational Agent Acquisition Program
  - Biobanking
  - Informatics
    - GeneGo Bioinformatics Tool MetaCore (pathway)
    - Eureka (database search)
    - MetaDrug
      - Compound based pathway analysis,
      - Systems pharmacology
      - Chemical biology

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

Project Development Teams → under Research Resources

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

- Voluntary review for support and suggestions with panel of experts, selected per protocol – basic and clinical science, ethics, regulatory, imaging, statistics, informatics, disease-specific, nursing.
- Specific recommendations – project manager to provide access to support, potential for consultations and collaborations.
- Funding suggestions and support (high success rate)
- Follow-up

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

- Specific resources/services – 100s of them
  - Phenotyping
  - Animal models/preservation of germ lines
  - Molecular modeling and design
  - 3-D copying
  - Electronic health record mining
  - Imaging, macro to micro to ultramicro
  - cGMP manufacture, cGCP clinical trials
  - Trained research coordinators, electronic protocol processing, case report forms

Access CTSA resources at sites, example: **https://www.indianactsi.org/**

- Questions?

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